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**A high dietary saturated fat is associated with insulin resistance in non-alcoholic steatohepatitis.**

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## P73

### HIGH PREVALENCE OF FOCAL NODULAR HYPERPLASIA (FNH) IN SUBJECTS WITH HEREDITARY HEMORRHAGIC TELANGIECTASIA (HHT): DOPPLER US STUDY

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**Background:** Literature suggests a possible vascular pathogenesis of FNH and its possible association with liver vascular malformation; we thus aimed this study to retrospectively evaluate in the cohort of subjects belonging to families with HHT and undergoing Doppler US study the prevalence of FNH, relating it to presence to stage of hepatic vascular derangement. **Methods:** Between 1990 and 4/2002 52 HHT families underwent a screening program including abdominal Doppler US. Two out major criteria (epistaxis, telangiectasia, well documented visceral involvement, autosomal dominant inheritance) had been required for a diagnosis of HHT. After 1997 the Curacao criteria have been applied for the diagnosis of HHT. By Doppler US we recorded: liver and spleen size, liver echostucture and margins. We studied caliber, course, flow patterns and abnormalities of the hepatic artery, portal vein and hepatic veins. Depending on the number and degree of abnormalities, we classified hepatic VMs as minimal, moderate and severe. Presence of liver focal lesions was recorded. Diagnosis of FNH was made if at least two examinations whether color Doppler sonography, liver scintigraphy, dynamic CT, RM showed suggestive findings. **Results:** FNH was found in 5 out of 274 subjects (1.8%); all five were affected by HHT, so the percentage related to the group of affected patients increases to 2.9; 4 of them presented severe liver VMs. Female to male ratio was 4:1. Mean age was 45 years; mean age of the female patients was 52. FNH was single in 3 cases; tumor size ranged between 26 and 120 mm. Diagnosis has been done by imaging in 4 cases; in 1 a biopsy has been done before our observation. In a mean follow up of 51.5 months 3 lesions remained unchanged, 1 showed increase, 1 FNH appeared during follow up. **Conclusions:** The prevalence of FNH in patients with HHT is 50 times greater than that reported in general population. Our observation confirm a possible vascular pathogenesis for FNH.

## P75

### FATTY LIVER, BLOOD LIPIDS AND HEPATIC BIOCHEMICAL PARAMETERS IN OBESE CHILDREN

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Childhood obesity is associated with high levels of total cholesterol and triglycerides. Asymptomatic liver involvement (most often steatosis and steatohepatitis) has recently been studied in obese children. The non-alcoholic steatohepatitis (NASH) is frequently diagnosed in obese patients and the ratio of alanine aminotransferase (ALT) to aspartate aminotransferase (AST) is almost always more than 1 in NASH. **Aim:** to study the association of fatty liver with anthropometric parameters, ratio ALT/AST, cholesterol and triglycerides levels in obese children. **Subjects and Methods:** forty-eight obese children (30 F), ranging from 7-14 y and BMI > 95<sup>th</sup> percentiles according to their age and sex, were enrolled. Anthropometric measurements: weight, height, body mass index (BMI), waist/hip ratio, bicipital (BP), tricipital (TP), subscapular (SS) and suprailiac (SP) skinfolds. Biochemical measurements: glucose, insulin, triglycerides, cholesterol, AST, ALT. Ultrasound examination (US) of the liver was scored for steatosis as follow: 0 = absent; 1 = weak; 2 = moderate; 3 = severe. **Results:** The US fatty liver score was weak in 30 (62.5%) and severe in 2 (4.2%) children. A positive correlation was present between anthropometric parameters and US liver score (BMI and US:  $r = 0.44$ ,  $p = 0.001$ ; SS and SP skinfolds and US:  $r = 0.33$ ,  $p = 0.01$ ;  $r = 0.32$ ,  $p = 0.02$  respectively); waist/hip ratio and US ( $r = 0.47$ ;  $p = 0.0008$ ). As regard biochemical data a positive correlation was present only between US and ALT/AST ratio ( $r = 0.50$ ;  $p = 0.001$ ). There were no significant relationship between triglycerides or cholesterol plasma levels and US. **Conclusions:** Although the diagnosis of NASH is usually based on liver histology, recently US has been widely used. As obesity has been identified as a major risk factor for the development of NASH, which is not a benign condition in adults and even in children, obese children should be evaluated for liver disease.

## P74

### EXPRESSION OF ESTROGEN RECEPTORS IN CHOLANGIOCYTES OF PATIENTS WITH PRIMARY BILIARY CIRRHOSIS (PBC)

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The expression of estrogen receptors (ER) in liver biopsies of patients with different stages of PBC and the relationship with immunohistochemical markers of cell proliferation and death were evaluated: Liver biopsies from post-menopausal normal females and female patients with PBC were investigated by histology and immunohistochemistry for ER-alpha and -beta, cytokeratin (CK)-19, PCNA, Tunel and degree of ductopenia. Serum samples were analyzed for liver biochemistry and estradiol serum levels (RIA-Kit). **Results:** estradiol serum levels were significantly ( $p < 0.05$ ) higher only in PBC stage IV in comparison with normal controls. Cholangiocytes of normal liver biopsies were negative for ER alpha and beta. In contrast, a significant immunohistochemical positivity for both ER-alpha and -beta was observed in cholangiocytes of PBC patients. The percent of cholangiocytes positive for ER-beta (50-65%) was similar among different stages of PBC. In contrast, the immunohistochemical positivity for ER-alpha progressively increased from stage I (1.2%) to stage III (12%) of PBC and was positively correlated with cell proliferation (PCNA,  $r = 0.77$ ;  $p < 0.01$ ). In PBC stage IV, ER-alpha was negative in cholangiocytes in association with the highest degree of ductopenia, with very high positivity for Tunel (apoptosis) and very low PCNA (proliferation) expression. **Conclusions:** Estrogen receptors are over-expressed in cholangiocytes of PBC patients. The expression of ER-alpha correlates with cholangiocyte proliferation. The terminal ductopenic stage of PBC is characterized by the disappearance of ER-alpha in association with enhanced apoptosis and impaired cell proliferation. These data suggest that estrogens and their receptors are involved in the regulation of cholangiocyte proliferation/death in the course of PBC.

## P76

### A HIGH DIETARY SATURATED FAT IS ASSOCIATED WITH INSULIN RESISTANCE IN NON-ALCOHOLIC STEATOHEPATITIS.

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**Background and aims.** Diet, particularly the amount and type of carbohydrate and fat, has been linked to insulin resistance and hepatic disease in different conditions. Data on alimentary habits of patients with NASH are lacking. Dietary habits and their relations to insulin sensitivity and liver enzymes were investigated in patients with non-alcoholic steatohepatitis (NASH) without type 2 diabetes, obesity or hyperlipidemia. **Material and methods.** Twenty-five NASH patients (24 males, age  $37 \pm 9$  yr, BMI  $25.6 \pm 2.5$  kg/m<sup>2</sup>) (mean  $\pm$  SD) and 25 age-, BMI- and gender-matched healthy controls underwent a 7-day daily alimentary record (data analyzed by WinFood database) and an oral glucose tolerance test (OGTT). The whole body insulin sensitivity index (ISI) was assessed from the OGTT. **Results.** Dietary intake of NASH patients was richer in total fat ( $39.1 \pm 4.8$  vs.  $31.1 \pm 5.2$  % kcal,  $p = 0.000$ ), saturated fat (SFA:  $13.7 \pm 3.1$  vs.  $10.0 \pm 2.1$  % kcal,  $p = 0.000$ ), and cholesterol ( $506 \pm 108$  vs.  $405 \pm 111$  mg,  $p = 0.002$ ) and poorer in polyunsaturated fat ( $10.0 \pm 3.5$  vs.  $14.5 \pm 4.0$  % total fat,  $p = 0.000$ ), antioxidant C ( $84.3 \pm 43.1$  vs.  $144.2 \pm 63.1$  mg,  $p = 0.000$ ) and E vitamin ( $5.4 \pm 1.9$  vs.  $8.7 \pm 2.9$  mg,  $p = 0.000$ ). The ISI was significantly lower in NASH patients than in controls ( $3.38 \pm 1.61$  vs.  $7.07 \pm 1.50$ ;  $p = 0.000$ ) and correlated with total calories ( $r_s = -0.51$ ;  $p = 0.013$ ) and SFA ( $r_s = -0.57$ ) but not with BMI or waist circumference. ALT levels correlated with ISI ( $r_s = -0.49$ ), total calories ( $r_s = 0.58$ ), SFA ( $r_s = 0.58$ ) and dietary polyunsaturated-to-saturated fat ratio ( $r_s = -0.50$ ). **Conclusions.** In conclusion, NASH group consumed a diet richer in SFA and poorer in polyunsaturated fat and antioxidant C and E vitamins; the causal role of these dietary habits and the benefit of their correction need to be further assessed.